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(21) International Application Number: PCT/SE92/00061 (22) International Filing Date: 4 February 1992 (04.02.92) (30) Priority data: 9100364-0 5 February 1991 (05.02.91) SE (71) Applicant (for all designated States except US): LECUR DEVELOPMENT IN SWEDEN AKTIEBOLAG [SE/SE]; Importgatan 1, S-262 73 Ängelholm (SE). (72) Inventor; and (75) Inventor/Applicant (for US only): KVANTA, Endre [SE/SE]; Mossvägen 22, S-262 61 Ängelholm (SE). (74) Agent: INGER, Lars, Ulf, Bosson; L&U Inger Patentbyrå AB, Garvaregatan 12, S-262 63 Ängelholm (SE).		(81) Designated States: AT (European patent), BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FI, FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), MC (European patent), NL (European patent), NO, SE (European patent), US. Published <i>With international search report.</i> <i>In English translation (filed in Swedish).</i>
(54) Title: TAMPON OR SANITARY NAPKIN PROVIDED WITH LACTIC ACID PRODUCING BACTERIA (57) Abstract <p>The present invention relates to a tampon or sanitary napkin to be used prophylactically against urogenital infections, as well as at acute or chronic urogenital infections in order to alleviate the effects of the infections, and contribute to a rapid recovery of the natural flora of microorganisms of the urogenital region after an antibiotic treatment, whereby the tampon or sanitary napkin is provided with a culture of at least one lactic acid producing bacteria particularly comprising the genus <i>Pediococcus</i>, preferably isolated from the urogenital region of healthy individuals.</p>		

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TAMPON OR SANITARY NAPKIN PROVIDED WITH LACTIC ACID PRODUCING BACTERIA

DESCRIPTION

Technical field

- 5 The present invention relates to the production and use of a tampon or sanitary napkin being impregnated with a culture of living lactic acid producing bacteria, preferably isolated from the genital region of healthy women with the object of alleviate or vaginal or urinary tract infections, alleviate or counteract the growth of undesired micro-organisms, alleviate or counteract vaginal discharge, the formation of odour producing secretion, as well as alleviate or counteract hygienic complaints caused by these as well as contribute to a more rapid recovery of the natural flora of lactic acid producing bacteria
- 10 of the urogenital region after an antibiotic treatment.

It is known that the urogenital region consists of a rich flora of micro organisms, preferably bacteria and fungi. It is also known that lactic acid producing bacteria of the Lactobacillus group dominates the micro flora of healthy women both prior to and after menopause and the most of these lactobacillus have an ability to sustain the growth and reduce the patogenicity of many uropathogens. The mechanism behind the antagonistic effect is not completely derived but the dominating comprehension is

20 that lactobacillus having antagonistic properties have an ability of coaggregate with the uropathogens, to produce inhibitors and to lower pH in the urogenital environment by the lactic acid production.

30 In connection with an infection of the urogenital region, UTI (Urogenital Tract Infection) a large increase of the number of uropathogens can be observed in the vagina and/or the urinary tract compared with healthy individuals.

35 It is also known that the antagonistic properties of lactobacillus and other lactic acid producing bacteria against pathogens is partly denoted their ability of producing different so

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called antimetabolites, such as lactic acid, hydrogen peroxide, bacteriocins, etc. One has also described how bacteriocins from lactobacillus seem to function against pathogens as bacteria and fungi.

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It is further known that one has tried to explore the antagonistic properties of the lactobacillus with the object of preventing urogenital infections. The literature describes e.g. that suspensions as well as suppositories comprising living lactobacillus have been used for this purpose. The same process has also been used for the purpose of being able to restore a natural vaginal flora more rapidly after a treatment of the urogenital region using antibiotics.

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It is also known that living lactobacillus packed in gelatine capsules have been used as well for that purpose. Such products are available now and then on the market, as well as suppositories.

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The problem of urogenital infections is great among women both prior to and after menopause. The troubles are widely spread. According to the literature up to 25% of all women will get an UTI some time during their lifetime, and more than 80% of these get repeated recidive. Urogenital infections not only cause a great suffering of those afflicted but cause also great economical consequences for the individual as well as for the public.

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UTI often requires long term antibiotic treatment. Up to two years of treatment using antibiotics is known from the literature. Most UTI can however, be cured after some months of antibiotic treatment. However, it is so that there are few possibilities to cure UTI if the patient is not willing to undergo a long term antibiotic treatment, due to the negative side effects which can be caused by the antibiotic therapy. As the use of antibiotic for prophylactic purpose not can be recommended and that the above methods to use viable lactobacillus either are regarded as nonhygienic, unesthetical or provide a small or

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no effect at all, the need is great to be able to use a prophylactic tool against urogenital infections in a cheap, simple and rational way.

- 5 It has turned out that this desire and the present problem can be met by best by means of the present invention, which is characterized in that a tampon or sanitary napkin is impregnated with viable cultures of lactic acid producing bacteria, particularly of the genus Pediococcus. The lactic acid producing bacteria to be used for this purpose shall show the following criteria. They shall preferably be naturally occurring in the urogenital region of healthy individuals, they shall have antagonistic properties against uropathogens, they shall be stable at cultivation and other technical handling, (i.e. they shall maintain their genetic properties in connection with or after a industrial production handling) and they shall be able to be administered in a lyophilized form.

- 20 The bacteria organisms that best meet these criteria belongs to the genus Pediococcus.

- 25 Comparative investigations made have also shown that bacteria belonging to the Lactobacillus group do not fulfil all these requirements. The primary reason to the uncertainty using Lactobacillus as an antagonistic micro-organism at UTI or against UTI is their well-known instability at a technical handling thereof. It has turned out that Lactobacillus per se provides an acceptable protection against urogenital infections as long as one uses the natural flora of Lactobacillus present of the respective individual. The desired antagonistic properties of the Lactobacillus, their genetic stability, the viability etc are, however, lost to a greater or less extent when they have been isolated from the naturally occurring environment and in connection with the subsequent technical handling thereof. The genetic instability of the Lactobacillus at technical handling is well-known and well documented. The Lactobacillus isolated from the genital tract or from the natural human intestinal

tract are hereby no exception.

Contrary to this it has turned out that pediococcus isolated from the genital tract keep stable during and after a necessary technical treatment, i.e. they maintain their genetic identity, their lactic acid producing ability, viability as well as the valuable antagonistic properties against uropathogens even after a long term storing.

10 By using pediococcus as a main organism at the impregnation of tampons or sanitary napkins according to the present invention we have succeeded in eliminating all practical problems which have inhibited a successful use of the previously proposed Lactobacillus.

15 As a further essential advantage using the present invention it can be mentioned that compared with lactobacillus the pediococcus are easily cultivated, have a rapid growth, high yield, and are readily handled at technical handling thereof.
20 These circumstances make the pediococcus also cheaper than the lactobacillus at the proposed use according to the present invention.

Impregnation of the tampon or sanitary napkin using freeze-dried viable lactic acid producing bacteria will be illustrated in the following non-restricting examples.

The term sanitary napkin shall mean sanitary napkin as well as any other means applied topically against the outer genitalia.

30 A tampon or sanitary napkin is coated with any compound having adhesive properties, such as coco fat, vegetabilic oil, or other glyceride or wax or any other compound having the similar properties and a good skin and mucous membrane tolerance at the use in the urogenital region. A culture of viable, freeze-dried bacteria is added then in such a way that the bacteria attach
35 on the coated area. The impregnated layer is then protected

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- with a permeable layer of a suitable material, e.g. the same material as having been used for the production of the tampon of sanitary napkin. When the tampon or sanitary napkin then become wet at the use thereof the bacteria become rehydrated in the fluid added and by natural diffusion they will thus migrate and establish in the urogenital region. It is also known that viable, freeze-dried lactic acid producing bacteria starts a logarithmic growth phase after some revitalization time.
- 10 Practical tests have shown that the use of a tampon or sanitary napkin impregnated with living viable lactic acid producing bacteria having the above given properties provides for a simple and efficient protection against UTI. It has also turned out that the same type of tampon or sanitary napkin can preferably be used not only prior to but even after menopause. It has also turned out that a tampon or sanitary napkin of the present invention can be used with a good result to rapidly restore the natural flora of micro-organisms of the urogenital region after an antibiotic treatment. It has also turned out to be important to use the right composition of the carrier of the lactic acid producing bacteria. As carrier of the freeze-dried lactic acid producing bacteria carbohydrates are suitably used which the bacteria can use for production of lactic acid, and essential growth promoting agents which facilitates the establishment of the urogenital region. It has thereby turned out that some B-vitamins are such growth promoting agents.

Lactic acid producing bacteria that are suitably used for this purpose are isolated from the genital region of healthy women and belong to the genera Pediococcus, Lactobacillus, but also Leuconostoc. Of the Pediococcus are primarily P. acidilacti, P. pentosaceus, P. urinae, and of the Lactobacillus; L. acidophilus, L. jensenii, L. casei, L. fermentum; and of the Leuconostoc: Les. mesenteroides.

The isolation process follows known routine processes for the isolation of pure cultures. The isolated pure cultures are then

typed according to known methods, e.g. API. The choice of suitable organisms is then made with regard to the desired properties, i.e. lactic acid production, and antagonistic properties against uropathogens. Thereby a choice of uropathogens representing uropathogen E. coli, Enterococcus but also those others actual pathogens belonging to staphylococcus, gonorrhea, Chlamydia, Trichosomas, Gardnerella, Bacterioides, Mobiluncus, Ureaplasma, Urealyticum, Klebsiella, Candida, and others known in connection with UTI are tested.

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The thus selected lactic acid producing bacteria are then cultivated in a fermentor in a manner known per se, are separated from the medium using a separator or a centrifuge, are freeze-dried in a manner known per se, and ground to a fine powder.

15 The powdery bacterial concentrate thus obtained is then mixed with a fermentable carbohydrate e.g. glucose, so that the final concentration of about 100 billion viable lactic acid producing bacteria per gram are obtained. This bacterial powder is then used to be added to a tampon or sanitary napkin in the above given way so that each tampon or sanitary napkin then contains about 100 mg powder, corresponding to >10 billion viable lactic acid producing bacteria.

25 The addition of the bacterial powder on a tampon or sanitary napkin can suitably be carried out in two ways. According to one method the tampon or sanitary napkin is coated with an adhesive according to above, and then a relevant amount of powder is then blown onto or spread over the coated place. The amount relationship between the main organism *Pediococcus* and other complementary lactic acid producing bacteria is of subordinated significance, however, at least 50% of the total amount of viable lactic acid producing bacteria should consist of *pediococcus*. Thereby the bacterial powder is attached to the basic layer. Then the tampon or sanitary napkin is provided with the above mentioned permeable layer of a suitable material in order to thus protect the bacterial layer against mechanical damage. It is also convenient to pack the tampon or sanitary

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napkin in a protecting film of tight paper, polymer film, aluminium foil or multiple layer foil. According to the second method the desired amount of bacterial powder is applied in the form of a suspension wherein the bacterial powder is finely distributed in the adhesive agent to a homogeneous suspension. The application can take place e.g. by coating of the suspension or by dipping the tampon in the suspension. In some cases it is also possible to add the living bacteria to a tampon or sanitary napkin and then carry out a freeze drying thereof.

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The tampon or sanitary napkin thus prepared has turned out to obstruct UTI, alleviate the troubles at acute and chronic UTI and to assist in a rapid recovery of the natural micro-organism flora of lactic acid producing bacteria after a antibiotic treatment.

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A group of women which are in particular sensitive to UTI are the pregnant women. At UTI in pregnant women it is thus not advisable to treat the infection using an antibiotic. Then one should use a tampon or sanitary napkin of the present invention in stead when such infections are at hand.

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CLAIMS

1. Tampon or sanitary napkin to be used prophylactically against urogenital infections, as well as at acute or chronic urogenital infections in order to alleviate the effects of the infections, and contribute to a rapid recovery of the natural flora of micro-organisms of the urogenital region after an antibiotic treatment, characterized in that the tampon or sanitary napkin is provided with a culture of at least one lactic acid producing bacteria particularly comprising the genus *Pediococcus*, preferably isolated from the urogenital region of healthy individuals.
2. Tampon or sanitary napkin according to claim 1, characterized in that the bacterial culture is retained onto the tampon or sanitary napkin using an adhesive.
3. Tampon or sanitary napkin according to claim 1 to 2, characterized in that the bacterial culture added optionally contains a combination of other lactic acid producing bacteria, such as *Lactobacillus* and *Leuconostoc*.
4. Tampon or sanitary napkin according to claim 1, characterized in that the active bacterial culture consist of *P. acidilacti*, *P. pentosaceus*, *P. urinae*, optionally in combination with one or more of the *Lactobacillus*, preferably *L. acidophilus*, *L. jensenii*, *L. casei*, *L. fermentum*; or of the *Leuconostoc*, preferably *Les. mesenteroides*.
5. Tampon or sanitary napkin according to claim 2, characterized in that the adhesive consist of coco fat, vegetabilic oil, other glyceride or wax.
6. Tampon or sanitary napkin according to claims 1 to 2, characterized in that the addition of lactic acid producing bacterial culture takes place in the form of a suspension consisting of an adhesive and lactic acid producing bacteria.

7. Tampon or sanitary napkin according to any of the preceeding claims, characterized in that the bacterial layer is coated with a permeable layer of cellulose fiber for protecting purposes.

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8. Tampon or sanitary napkin according to claims 1 to 7, characterized in that it is provided with a non-permeable protecting layer of polymer or other foil applied above the permeable layer.

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9. Tampon or sanitary napkin according to claim 3, characterized in that the amount of bacteria added is at least 10^4 and at most 50×10^9 per unit.

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INTERNATIONAL SEARCH REPORT

International Application No PCT/SE 92/00061

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: A 61 L 15/36, A 61 F 13/15																	
II. FIELDS SEARCHED <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black;">Minimum Documentation Searched⁷</div> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 25%; border-bottom: 1px solid black;">Classification System</td> <td style="border-bottom: 1px solid black;">Classification Symbols</td> </tr> <tr> <td style="height: 40px; vertical-align: bottom;">IPC5</td> <td style="height: 40px; vertical-align: bottom;">A 61 L</td> </tr> </table>			Classification System	Classification Symbols	IPC5	A 61 L											
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Documentation Searched other than Minimum Documentation to the extent that such Documents are included in Fields Searched ⁸ SE,DK,FI,NO classes as above																	
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%;">Category¹⁰</th> <th style="width: 60%;">Citation of Document¹¹ with indication, where appropriate, of the relevant passages¹²</th> <th style="width: 30%;">Relevant to Claim No.¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">A</td> <td>SE, A, 8505491-4 (HANDELSBOLAGET PER OCH PIA EDLUND) 20 November 1985, see the whole document ---</td> <td style="text-align: center;">1-9</td> </tr> <tr> <td style="text-align: center;">A</td> <td>DE, A, 2309575 (WENDERLEIN, J. MATTHIAS) 5 September 1974, see the whole document ---</td> <td style="text-align: center;">1-9</td> </tr> <tr> <td style="text-align: center;">A</td> <td>GB, A, 2107192 (UNIVERSITY OF DELAWARE) 27 April 1983, see the whole document ---</td> <td style="text-align: center;">1-9</td> </tr> <tr> <td style="text-align: center;">A</td> <td>EP, A1, 0130356 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN) 9 January 1985, see the whole document -----</td> <td style="text-align: center;">1-9</td> </tr> </tbody> </table>			Category ¹⁰	Citation of Document ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	A	SE, A, 8505491-4 (HANDELSBOLAGET PER OCH PIA EDLUND) 20 November 1985, see the whole document ---	1-9	A	DE, A, 2309575 (WENDERLEIN, J. MATTHIAS) 5 September 1974, see the whole document ---	1-9	A	GB, A, 2107192 (UNIVERSITY OF DELAWARE) 27 April 1983, see the whole document ---	1-9	A	EP, A1, 0130356 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN) 9 January 1985, see the whole document -----	1-9
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<div style="display: flex; justify-content: space-between;"> <div style="width: 48%;"> <p>* Special categories of cited documents:¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 48%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, each combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>																	
IV. CERTIFICATION <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; border-bottom: 1px solid black;">Date of the Actual Completion of the International Search</td> <td style="width: 50%; border-bottom: 1px solid black;">Date of Mailing of this International Search Report</td> </tr> <tr> <td style="height: 30px; vertical-align: bottom;">19th May 1992</td> <td style="height: 30px; vertical-align: bottom;">1992 -05- 22</td> </tr> <tr> <td style="border-bottom: 1px solid black;">International Searching Authority</td> <td style="border-bottom: 1px solid black;">Signature of Authorized Officer</td> </tr> <tr> <td style="height: 30px; vertical-align: bottom; text-align: center;">SWEDISH PATENT OFFICE</td> <td style="height: 30px; vertical-align: bottom; text-align: center;"> <i>Sofia Nikolopoulou</i> Sofia Nikolopoulou </td> </tr> </table>			Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	19th May 1992	1992 -05- 22	International Searching Authority	Signature of Authorized Officer	SWEDISH PATENT OFFICE	<i>Sofia Nikolopoulou</i> Sofia Nikolopoulou							
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**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. PCT/SE 92/00061**

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
SE-A- 8505491-4	85-11-20	NONE	
DE-A- 2309575	74-09-05	NONE	
GB-A- 2107192	83-04-27	DE-A- 3236768	83-04-21
		FR-A- 2513875	83-04-08
		JP-A- 58075548	83-05-07
		US-A- 4431427	84-02-14
EP-A1- 0130356	85-01-09	DE-A- 3320218	84-12-06
		JP-A- 60005149	85-01-11